J Korean Surg Soc 2013;84:298-303
http://dx.doi.org/10.4174/jkss.2013.84.5.298

JKSS
Journal of the Korean Surgical Society

pISSN 2233-7903 · eISSN 2093-0488

ORIGINAL ARTICLE

Prevention of venous thromboembolism with enoxaparin in bariatirc surgery

Hee Doo Woo, Yong Jin Kim

Department of Surgery, Soonchunhyang University College of Medicine, Seoul, Korea

Purpose: Venous thromboembolism (VTE) after bariatric surgery is a significant cause of morbidity and mortality. Current modalities of thromboprophylaxis include subcutaneous injection of unfractionated or low-molecular-weight heparin (LMWH), pneumatic compression, elastic stockings, and inferior vena cava filters. Despite universal agreement on the need for thromboprophylaxis, no clear consensus has been reached regarding the best regimen and treatment duration of bariatric surgery. **Methods:** From April, 2009 to December, 2011, we performed 200 bariatric surgery (191 with primary intent, 9 with revisional intent). There was no history of VTE prior to surgery. Clexane therapy was done with 4000 U SQ once daily for 2 weeks to the day before surgery. Development of VTE was assessed by direct interview, physical examination in out-patient clinic, and phone calls to patients for history taking if needed. The history taking was presented in questionnaire format. The patients were asked to state their symptoms of VTE by answering the questionnaire. The patients were followed up for a minimum of 6 months after surgery to determine the incidence of clinical VTE. **Results:** Two-week Clexane therapy was completed in 193 patients. Clexane was stopped in 5 due to surgical related complications (4 bleeding, 1 reoperation due to leak), in 2 due to Clexane related complications (1 epistaxis, 1 metrorrhagia). Follow-up of out-patient clinic were 68%, those who could follow up by telephone were 89%. There was no evidence of VTE. **Conclusion:** A 2-week VTE prophylaxis regimen using LMWH is simple, effective and associated with a low incidence of complications.

Key Words: Venous thromboembolism, Bariatric surgery, Low-molecular-weight heparin

INTRODUCTION

Venous thromboembolism (VTE) is a disease that encompasses the diagnosis of deep vein thrombosis (DVT) and pulmonary embolism (PE). Despite being a preventable problem, VTE has a high prevalence. Without prophylaxis, the incidence of hospital-acquired DVT is approximately 10% to 40% among medical or general surgery patients and 40% to 60% following major surgery [1]. Also, approximately 10% of hospital deaths are caused by PE [1,2]. The effectiveness of primary thromboprophylaxis, to reduce the frequency of DVT and PE, is supported by well-established scientific evidence. Heparin products that include unfractionated heparin (UH), low-molecular-weight heparin (LMWH), and vitamin K antagonists are the most commonly used prophylactic treatments that have demonstrated good efficacy and cost effectiveness [1]. While these agents have been used for many years,

Received December 24, 2012, Revised February 5, 2013, Accepted February 20, 2013

Correspondence to: Yong Jin Kim
Department of Surgery, Soonchunhyang University Seoul Hospital, 59 Daesagwan-ro, Yongsan-gu, Seoul 140-743, Korea
Tel: +82-2-709-9479, Fax: +82-2-795-1687, E-mail: yjgs1997@gmail.com

each class has its drawbacks and are far from being "ideal" anticoagulants [2]. VTE is feared by most surgeons performing weight loss surgery because of the perception of greater risk for the severely obese patient. VTE is considered one of the major causes of mortality for patients undergoing bariatric surgery with an incidence of DVT and PE of 1–3% and 0.3–2%, respectively. The mortality of those patients with PE has been reported to be as great as 30% [3-5].

Although the incidence of VTE has been modest, the widespread increase in bariatric surgery and the adoption of laparoscopic techniques could lead to a relatively large number of patients developing, and possibly dying of, VTE [4,5]. Because these are potentially preventable deaths, primary prevention is the key to reducing the morbidity and mortality of VTE.

Despite universal agreement on the need for thromboprophylaxis, no clear consensus has been reached regarding the best regimen and treatment duration. Current modalities of thromboprophylaxis include subcutaneous injection of unfractionated or low molecular weight heparin, pneumatic compression devices, elastic stockings, and inferior vena cava filters [5,6]. It is certain that prophylaxis has to be given in bariatric surgery patients [6]. However, the optimal dose, the timing and the duration of the treatment are still unknown. Some regimens consist of UH given 5,000 IU subcutaneously every 8 hours or enoxaparin 30 to 40 mg subcutaneously every 12 hours. Some groups have increased the LMWH dose up to 60 mg twice daily but some bleeding complications have occurred. The duration of the treatment is also unknown, even if it appears that expending pharmacological prophylaxis after discharge for 1 or 2 weeks is well tolerated and effective [7-9].

For this reason, the aim of our study was to identify the effects and complications of clinical postoperative VTE in morbidly obese patients undergoing laparoscopic bariatric surgery in a 2-week VTE prophylaxis regimen using LMWH.

METHODS

This study was approved by the Institutional Review Board for human investigation of Soonchunhyang University Seoul Hospital. The patients were studied retrospectively from a prospective database from April, 2009 to December, 2011. We identified all patients with a minimum of 6 months of follow-up who had undergone a laparoscopic bariatric procedure (i.e., laparoscopic adjustable gastric banding, laparoscopic Roux-en-Y gastric bypass, laparoscopic sleeve gastrectomy). There was no history of VTE prior to surgery. A protocol of thromboprophylaxis was followed. Patients received Clexane 4,000 IU subcutaneously once daily for 2 weeks. The patients were trained to self-administer the injections before discharge. Before discharge from the hospital, we gave information on using Clexane and methods to every patient, and we checked the patients who used Clexane 4,000 IU subcutaneously once daily for 2 weeks in the out-patient clinic after 2 weeks. Early mobilization from the postoperative day was mandatory. Whole leg compression stockings and pneumatic compression devices were also used during the hospitalization periods. This protocol was consecutively used in 200 patients who had bariatric surgery in Soonchunhyang University Seoul Hospital.

Patients were given their first follow-up appointment 2 weeks after surgery and were subsequently reviewed one month, 3 months, and 6 months after surgery. The patients were followed up for a minimum of 6 months after surgery to determine the incidence of clinical VTE. Development of VTE was assessed by direct interview and physical examination in out-patient clinic and phone calls to the patients for history taking if needed. The history taking was presented in questionnaire format. The patients were asked to state their symptoms about VTE by answering the questionnaire. The symptom of the VTE is such as if the patients had dyspnea, chest pain, hemoptysis, leg swelling, calf pain (Suppl. 1).

The following data were extracted from the medical records of all patients: age, gender, body mass index (BMI), previous abdominal surgery, bariatric surgical procedure, hospital stays, morbidity, and previous VTE.

Three different types of bariatric surgery were performed, Roux-en-Y gastric bypass, gastric banding, and sleeve gastrectomy. All procedures were performed laparoscopically, and there was no open conversion. Gastric

bypass was performed in an antecolic, antegastric Roux-en-Y manner to an approximately 30 mL gastric pouch with the bilioenteric limb measuring 50 to 100 cm and the alimentary limb measuring 75 to 150 cm. The anastomoses were stapled. Gastric banding involved a pars flaccida approach and fixation of the band with anterior gastropexy. Sleeve gastrectomy was constructed after full mobilization of the body and fundus of the stomach over a 34 Fr orogastric tube with stapler division beginning 4 to 6 cm from the pylorus.

RESULTS

The study population consisted of 200 cases that there were 191 primary cases and 9 revision cases. In primary cases, laparoscopic adjustable banding were 4 cases, laparoscopic sleeve gastrectomy were 132 cases, and laparoscopic Roux-en-Y gastric bypass were 55 cases. The revision operations were 9 cases consisting of 3 laparoscopic sleeve gastectomies and 6 laparoscopic Roux-en-Y gastric bypasses (Table 1). The patients' mean age was 35 years (range, 14 to 63 years). Male to female ratio was 32 versus 168, and mean weight was 105 kg with mean BMI of 39 kg/m². Major complications were 10 cases (5%), reoperations were 4 cases (2%) (Table 2). The number of patients who had diabetes mellitus was 27%, hypertension was 34% (Table 3).

One hundred ninety-three patients completed a 2-week Clexane therapy (97%). Clexane was stopped in 7 patients. Among them, 5 patients had surgical related complication. 4 patients had intra-abdominal bleeding and 1 patient had reoperation due to leak. Among 4 bleeding patients, two patients stopped bleeding without transfusion. And the other two patients had reoperation. In those two cases, bleeding was stopped by reoperation. Two patients had potentially Clexane related problems. One patient had epistaxis and needed electric cautery to stop bleeding, and 1 patient had metrorrhagia needing oxytocin to stop bleeding (Table 4). Epistaxis and metrorrhagia occurred after 2 weeks from operation.

Mean follow-up periods was 9 months. We lost follow up in 12 patients (6%). More than 6 months follow-up of outpatient clinic was with 136 patients (68%), and more than 6 months follow-up of outpatient clinic and phone call was with 177 patients (89%). The overall incidence of symptomatic postoperative VTE was 0%.

Table 1. The types of surgery (n = 200)

The types of surgery	No.
Primary	191
Laparoscopic adjustable banding	4
Laparoscopic sleeve gastrectomy	132
Laparoscopic Roux-en-Y gastric bypass	55
Revision	9
Laparoscopic sleeve gastrectomy	3
Laparoscopic Roux-en-Y gastric bypass	6

Table 2. Demographics of the obesity patients

Demographic	Value
Age (yr)	35 (14–63)
Male to female ratio	32:168
Weight (kg)	105 (64–212)
Body mass index (kg/m^2)	39 (24–70)
Operation time (min)	118 (45–340)
Hospital stay (day)	3 (1–82)

Values are presented as mean (range).

Table 3. Patients comorbidities

Patients comorbidity	No. (%)
Diabetes mellitus	54 (27)
Hypertension	68 (34)
Dyslipidemia	98 (49)
Sleep apnea	44 (22)
Degenerative joint disease	56 (28)
Disorder of menstruation	32 (16)

Table 4. Complication of clinical course of thromboprophylaxis

Complication	No. (%)
Take obesity surgery	200
Complete 2-week therapy	193 (96.5)
Stopped therapy	7 (3.5)
Surgical related problem	5 (2.5)
Bleeding	4 (2.0)
Reoperation due to leak	1 (0.5)
Clexane related problem	2 (1.0)
Epistaxis	1 (0.5)
Metrorrhagia	1 (0.5)

DISCUSSION

The results of the present study have shown that within an active thromboprophylaxis program that includes additional measures for higher risk patients, laparoscopic bariatric surgery is associated with a low incidence of clinical VTE. But no consensus has yet been reached on the prophylactic regimen or the optimal LMWH dose and the duration for prophylaxis in the patients undergoing laparoscopic bariatric surgery [7-10]. Hamad et al. [10] described the dose and the duration of LMWH used in this study varied among the study centers. There are few data from randomized controlled trials to determine the optimal prophylactic dose of LMWH in obese patients undergoing bariatric surgery. Kalfarentzos et al. [11] randomly assigned 60 gastric bypass patients to two different doses of LMWH. The lower dose of 5,700 IU was as effective as the 9,500 IU dose and was associated with fewer bleeding complications. Two studies have questioned the use of a fixed dose, as opposed to a weight-based (mg/kg) dose of LMWH in obese patients [12,13]. Frederiksen et al. [14] demonstrated a strong negative correlation between body weight and the anticoagulant effect of a fixed dose of enoxaparin (40 mg) [15-17].

In one study of 1,025 patients who underwent laparoscopic or open gastric bypass, those who bled were significantly more likely to have received preoperative LMWH versus no VTE prophylaxis for major colon and rectal surgery; LMWH significantly reduce the risk of postoperative VTE but was associated with a significantly greater rate of bleeding-related complications [12,18,19]. Scholten et al. [20] observed bleeding of 0.3% and 1.1% in patients receiving LMWH 40 mg q 12 hours and 30 mg q 12 hours, respectively. In our study, 193 patients were completed 2-week Clexane therapy (97%). Clexane was stopped in 7 patients due to complications (3%). Four patients had bleeding and 1 patient had reoperation due to leak. Four patients had intraluminal bleeding; among them, two patients stopped bleeding without transfusion, two patients had reoperation. In the latter two cases, bleeding was stopped at the time of reoperation. However, we thought that the bleeding focus of one was on the remnant stomach stapler line, and the other near the mesentery. Yet we could not exclude the cause of bleeding being due to using Clexane, but in every four cases, this bleeding happened on operation day, so we decided that this bleeding is related to the operation itself, not Clexane therapy. In addition, 2 patients had potential Clexane related problems. One patient had epistaxis, and 1 patient had metrorrhagia. There was no severe major bleeding in our study. Also, there was no development of symptomatic VTE. As judged from our study, the problem with thromboembolic complications after obesity surgery seems to be small and infrequent. There are only two prospective studies in the literature on the incidence of thromboembolic disease after obesity surgery using objective testing in addition to the present study [21]. As judged from these studies, thromboembolic complications appear to be rare after obesity surgery.

Most of bariatric surgeons still use mechanical devices such as sequential compression devices in conjunction with a type of heparin [7-10]. Chemical prophylaxis used alone has not been proved to be superior to the use of mechanical devices as prophylaxis against DVT, and some have suggested that the addition of heparin to mechanical devices are used appropriately $<50\%$ of the time when indicated for a patient, despite being properly ordered [7,22]. Therefore, the use or addition of a type of heparin in addition to mechanical devices seems justified. For this reason, in our study, whole-leg compression stockings and pneumatic compression devices were also used.

A minimum of 6 months follow-up for the analysis of VTE incidence was chosen because the published data have suggested that at that point the risk of postoperative VTE should have return to the basal level. Furthermore, 6 months postoperatively, significant weight loss has usually occurred, thereby reducing the risk of VTE further [22,23].

We accept that our study probably underestimated the true incidence of postoperative VTE after laparoscopic bariatric surgery, because we only included symptomatic patients in our analysis and did not routinely screen for silent VTE using duplex ultrasonography or plethysmography. However, given the low-recorded incidence of VTE in bariatric patients, the cost/benefit advantage of such

screening would have been dubious, because it would be unlikely to detect DVTs of clinical significance [21-23].

The limitation of this study is that it is a retrospective design with no randomization. Further, long-term follow-up is necessary to evaluate VTE. Indeed, to establish a consensus guideline for LMWH prophylaxis treatment, a large-scale prospective randomized study is necessary.

In conclusion, the results of our study have demonstrated that a 2-week VTE prophylaxis regimen using LMWH after bariatric surgery is both simple and effective, is safe with very low incidence of VTE and bleeding complications.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

SUPPLEMENTARY MATERIALS

Supplementary material can be found via http://thesurgery.or.kr/src/sm/jkss-84-298-s001.pdf.

REFERENCES

1. Montoya RC, Gajra A. Current status of new anticoagulants in the management of venous thromboembolism. Adv Hematol 2012;2012:856341.
2. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(6 Suppl):381S-453S.
3. Sapala JA, Wood MH, Schuhknecht MP, Sapala MA. Fatal pulmonary embolism after bariatric operations for morbid obesity: a 24-year retrospective analysis. Obes Surg 2003; 13:819-25.
4. Wu EC, Barba CA. Current practices in the prophylaxis of venous thromboembolism in bariatric surgery. Obes Surg 2000;10:7-13.
5. Magee CJ, Barry J, Javed S, Macadam R, Kerrigan D. Extended thromboprophylaxis reduces incidence of postoperative venous thromboembolism in laparoscopic bariatric surgery. Surg Obes Relat Dis 2010;6:322-5.
6. Bergqvist D, Agnelli G, Cohen AT, Eldor A, Nilsson PE, Le Moigne-Amrani A, et al. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. N Engl J Med 2002;346:975-80.
7. Barba CA, Harrington C, Loewen M. Status of venous thromboembolism prophylaxis among bariatric surgeons: have we changed our practice during the past decade? Surg Obes Relat Dis 2009;5:352-6.
8. Samama CM, Godier A. Perioperative deep vein thrombosis prevention: what works, what does not work and does it improve outcome? Curr Opin Anaesthesiol 2011;24: 166-70.
9. Rocha AT, de Vasconcellos AG, da Luz Neto ER, Araujo DM, Alves ES, Lopes AA. Risk of venous thromboembolism and efficacy of thromboprophylaxis in hospitalized obese medical patients and in obese patients undergoing bariatric surgery. Obes Surg 2006;16:1645-55.
10. Hamad GG, Choban PS. Enoxaparin for thromboprophylaxis in morbidly obese patients undergoing bariatric surgery: findings of the prophylaxis against VTE outcomes in bariatric surgery patients receiving exnoxaparin (PROBE) study. Obes Surg 2005;15:1366-74.
11. Kalfarentzos F, Stavropoulou F, Yarmenitis S, Kehagias I, Karamesini M, Dimitrakopoulos A, et al. Prophylaxis of venous thromboembolism using two different doses of low-molecular-weight heparin (nadroparin) in bariatric surgery: a prospective randomized trial. Obes Surg 2001;11:670-6.
12. Gonzalez QH, Tishler DS, Plata-Munoz JJ, Bondora A, Vickers SM, Leath T, et al. Incidence of clinically evident deep venous thrombosis after laparoscopic Roux-en-Y gastric bypass. Surg Endosc 2004;18:1082-4.
13. Chan MM, Hamza N, Ammori BJ. Duration of surgery independently influences risk of venous thromboembolism after laparoscopic bariatric surgery. Surg Obes Relat Dis 2013;9:88-93.
14. Frederiksen SG, Hedenbro JL, Norgren L. Enoxaparin effect depends on body-weight and current doses may be inadequate in obese patients. Br J Surg 2003;90:547-8.
15. House of Commons Health Committee. The prevention of venous thromboembolism in hospitalized patients. London: The Stationery Office Ltd.; 2005. p.3.
16. Bazinet A, Almanric K, Brunet C, Turcotte I, Martineau J, Caron S, et al. Dosage of enoxaparin among obese and renal impairment patients. Thromb Res 2005;116:41-50.
17. Ojo P, Asiyanbola B, Valin E, Reinhold R. Post discharge prophylactic anticoagulation in gastric bypass patient-how safe? Obes Surg 2008;18:791-6.
18. Hirsh J, Raschke R. Heparin and low-molecular-weight heparin: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126(3 Suppl): 188S-203S.
19. Westling A, Bergqvist D, Bostrom A, Karacagil S, Gustavsson S. Incidence of deep venous thrombosis in patients undergoing obesity surgery. World J Surg 2002; 26:470-3.
20. Scholten DJ, Hoedema RM, Scholten SE. A comparison of two different prophylactic dose regimens of low molecular

weight heparin in bariatric surgery. Obes Surg 2002;12: 19-24.
21. Raftopoulos I, Martindale C, Cronin A, Steinberg J. The effect of extended post-discharge chemical thromboprophylaxis on venous thromboembolism rates after bariatric surgery: a prospective comparison trial. Surg Endosc 2008; 22:2384-91.
22. Hamad GG, Choban PS. Enoxaparin for thromboprophylaxis in morbidly obese patients undergoing bariatric surgery: Findings of the prophylaxis against WE outcomes in bariatric surgery patients receiving enoxaparin (PROBE) study. Obes Surg 2005;15:1368-74.
23. Frezza EE, Chiriva-Internati M. Venous thromboembolism in morbid obesity and trauma: a review of literature. Minerva Chir 2005;60:391-9.